REMARKS

First of all applicants apologize for the incorrect citations provided the last response regarding the support for the submitted claim amendments, and for any hardship those incorrect citations caused. In addition, applicants wish to express their gratitude for the courtesies extended to the undersigned attorney during the telephonic interview conducted on December 15, 2005. During that interview applicants discussed the recently cited Fields patent application (WO 95/21382) and the failure of that reference to teach a device having a thermal cycling chamber that also houses a carousel and fluorescence detection system.

The claims have been amended to address the Examiner's rejections in the Office Action dated November 14, 2005 and to place the claims in condition for allowance, or in better form for appeal. Applicants acknowledge that these amendments are being made after final rejection and that entry of amendments after final are made at the Examiner's discretion. The amendments to the claims are believed to be responsive to the Examiner's most recent rejections, and applicants respectfully request their entry.

The claims have been amended to more clearly define that which applicants believe to be their invention. More particularly, claims 13, 33, 55, 128, 145, 152, 173, and 194 have been amended to specify that the carousel and the monitoring position are located within the same chamber used to conduct PCR. This arrangement of elements allows for the monitoring of the individual reactions during the amplification reaction. Support for these amendments is found throughout the specification and more particularly in Figures 11, 21, 27, 28 and 29, in previously submitted claims 79, 122 and 147 and on page 64, line 6 through page 66, line 20 (more particularly, page 66, lines 8-11). Claims 13, 33, 82, 121, 128, 145 and 173 have been amended to specify that the sample containers are formed for holding a maximum volume of 1 milliliter of a sample. Support for these amendments is found on page 106, lines 13-17.

The Examiner has noted that the present claimed invention is not given priority to parent application 08/658,993. Applicants respectfully submit the presently claimed invention is supported by US patent application no. 08/658, 993 and refer the Examiner to originally filed claim 3 as well as page 57, lines 4-6 and the drawings of the 08/658, 993 application. US patent application no. 08/658, 993 describes the use of a carousel in a thermal cycling device in conjunction with real time monitoring of the samples.

Accompanying this Response is a Disclaimer of Priority wherein applicants have disclaimed the previously claimed priority to U.S. Patent Application Serial No. 08/537,612, filed October 2, 1995, U.S. Patent Application Serial No. 08/179, 969, filed January 10, 1994, U.S. patent application Ser. No. 07/815,966 filed Jan. 2, 1992, and U.S. patent application Ser. No. 07/534,029 filed Jun. 4, 1990. Accordingly, Applicants request the record to be corrected to indicate that the application now claims priority only to U.S. Patent Application Serial No. 08/658,993, filed June 4, 1996, entitled System and Method for Monitoring PCR Processes.

The Examiner contends that several of the claims require interpretation. Applicants respectfully submit that the claim language speaks for itself. However, to expedite the prosecution of this application and provide further clarity, applicants have amended claims 13, 33, 82, 121, 128, 145 and 173 to specify that the sample containers are formed for holding a maximum volume of 1 milliliter of a sample.

Allowable Subject Matter

Applicants acknowledge that the Examiner has found claims 152 and 154-155 allowable. Claims 126, 127, 149 and 150 are objected to as dependent upon rejected claims.

35 USC §102 Rejections

Claims 13-18, 20-35, 55-57, 82, 121-125, 128-132, 134,-140, 145-148, 151, 156-158, 160, 169-195 and 197 stand rejected under 35 USC § 102, as being anticipated by Fields et al (WO95/21382). Applicants respectfully traverse.

As discussed during the Examiner's interview conducted on December 15, 2005, the present invention is directed to a device that has been configured to allow real time fluorescent monitoring of multiple PCR reactions during amplification. To accomplish this, the device has been configured to comprise a chamber for conducting thermal cycling reactions (a thermal cycling chamber) wherein the chamber further includes a carousel, as well as means for fluorescently exciting and detecting fluorescence from samples held in the carousel while the samples are being thermally cycled. Applicants respectfully submit that the previously submitted claims already required the carousel to be present in the thermal cycling chamber at the time of the fluorescent monitoring, since the claims stated that fluorescence of the excited sample is to be detected during amplification. However, to

expedite the prosecution of this application, and to further clarify the present claims, applicants have amended the claims to explicitly state the location of these elements.

More particularly, independent claims 13, 33, 55, 128, 145, 173 and 194 have been amended to state that the device comprises a chamber, wherein a carousel is rotatably mounted in the chamber and moves the samples to a monitoring position, said monitoring position also being located within the chamber. The amended claims further recite that the samples are subjected to thermal cycling while in the chamber and each sample is subjected to fluorescent monitoring when in the sample is in the monitoring position. See Fig. 21 showing a sample vessel (450) being held within a carousel (480) and being subjected to thermal cycling while being fluorescently monitored when in the monitoring position as indicated on the left side of the drawing.

Applicants note that previously submitted claims 79, 82, 121, 147 and 152 already contain language specifically reciting that the device comprises a chamber having a carousel rotatably mounted within the chamber and fluorescent monitoring means for monitoring samples within the chamber. Therefore applicants respectfully submit the presently submitted claim amendments raise no new issues of patentability.

The Fields reference fails to teach or suggest a device comprising a single chamber that contains a carousel and means for monitoring the samples within the thermal cycling chamber. Throughout the entire 94 page document, Fields makes only one reference to a "carousel dispensing device." No further characterizations of the carousel dispensing device are provided, nor are there any figures demonstrating what applicants had envisioned by such a device. However, Fields does clearly state that the "carousel dispensing device" is to be used in conjunction with the sample tube reader. As indicated on page 28, lines 7-9 and 24-25, and Fig. 10 of the Field disclosure, the sample tube reader (557) is a compartment separate and distinct from the thermal cycling chamber (555). Therefore the "carousel dispensing device" as disclosed by Fields is used in a chamber separate from the thermal cycling chamber. Thus Fields fails to teach a device comprising a thermal cycling chamber that includes a carousel that moves multiple samples to a fluorescent monitoring position, wherein the monitoring position is also located within the chamber.

Advantageously, applicants' unique arrangement of elements allows for real time fluorescent monitoring of a PCR amplification. Fields is devoid of any teaching or suggestion that the sample vessels can be fluorescently monitored during the amplification

reaction. On the contrary, Fields repeatedly states that fluorescent monitoring of their samples is conducted as a separate step, in a separate compartment, and not while the samples are being subjected to thermal cycling (for example, see page 35, lines 16-19, page 38, lines 12-15, page 39, lines 10-13 and lines 31-34). Thus Fields requires the removal of the samples from the thermal cycling compartment for fluorescent analysis.

Fields fails to teach applicants' device that provides a novel combination of elements to allow for real time monitoring of samples (i.e. monitoring the samples while they are being subjected to thermal cycling). Accordingly applicants request the withdrawal of the rejection of claims 13-18, 20-35, 55-57, 82, 121-125, 128-132, 134,-140, 145-148, 151, 156-158, 160, 169-195 and 197 as being anticipated by Fields et al (WO95/21382). In addition applicants respectfully submit that claims 126, 127, 149 and 150 are also patentable without further amendment of those claims.

35 USC §103 Rejections

Claims 58 and 59 stand rejected under 35 USC § 103 as being unpatentable over Fields et al. in view of Mitoma et al. Applicants respectfully traverse.

Claims 58 and 59 ultimately depend from claim 55. As noted above, the Fields reference fails to teach or suggest the invention of claim 55. The Mitoma reference fails to supplement the inadequacies of the Fields reference with regards to a device comprising a thermal cycling chamber that contains a rotatable carousel. Accordingly, applicants respectfully submit that dependent claims 58 and 59 are patentable over the combined teachings of Fields et al. in view of Mitoma et al.

Claims 79 and 80 stand rejected under 35 USC § 103 as being unpatentable over Fields et al. in view of Donohue (US Patent No: 5,311,426). Applicants respectfully traverse.

The deficiencies of the Fields disclosure have already been discussed above. Donohue is directed to an apparatus for conducting a plurality of enzyme immuno assays and automated means for measuring the results of those assays. The Donohue reference discloses an apparatus comprising a carousel and an optical reader for detecting the presence of a labeled capture reagent. Donohue fails to teach or suggest a device comprising a thermal cycling chamber. Nor does that reference provide any motivation for providing means to thermally cycle the contents of the device's chamber.

Applicants respectfully submit there is no motivation for combining the teachings of Fields and Donohue. Fields is directed to a device for conducting PCR amplifications, requiring the use of a thermal cycling chamber, whereas Donohue is directed to an automated immuno assay analyzer. Furthermore, since neither Donohue or Fields discuss the desirability of conducting real time fluorescent monitoring of samples (i.e. fluorescence monitoring during the reaction) there is no motivation to modify the device disclosed by Fields to include a carousel that moves the samples to a monitoring position within the thermal cycling chamber.

The present invention is directed to a system comprising multiple elements that have been selected, and combined in a unique fashion, to provide a system that rapidly and homogenously heats and then cools a sample multiple times (i.e. rapid thermal cycling) while allowing monitoring of multiple PCR amplifications during the amplification reaction. In particular, applicants' system allows for unimpeded air flow to each of the samples (whether or not they are present in the monitoring position) while allowing the monitoring of the samples during PCR amplification. The complexities involved in conducting fluorescent monitoring of samples while they are being rapidly thermal cycled in a homogenous manner is not addressed by the cited references, nor is any motivation provided by those references that would induce one to attempt to make modification to the Fields device to allow monitoring of the samples while they are thermally cycled. Accordingly, applicants respectfully submit the claimed invention is patentable over the cited references and request the withdrawal of the rejection of claims 79 and 80 as being unpatentable over Fields et al. in view of Donohue

The foregoing claim amendments and remarks are believed to fully respond to the Examiner's rejections. The claims are believed to be in condition for allowance. Applicants respectfully request allowance of the claims, and passage of the application to issuance.

Respectfully submitted,

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